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EXAMINER
HINES, JANA A

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Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/306,780	Applicant(s) TAKEMURA ET AL.	
	Examiner Ja-Na A Hines	Art Unit 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 February 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-40* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-40* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Amendment Entry

1 The amendment filed February 11, 2002 has been entered. Claims 17-24 have been canceled. Claims 25 and 31-32 have been amended. Claims 33-40 have been added. Claims 25-40 are under consideration in the office action.

Withdrawal of Rejections

2. The rejection of claims 23 and 24 under 35 U.S.C. 103(a) as being unpatentable over Takahara et al., in view of Weiner et al., in further view of Ono et al. is withdrawn in view of applicants amendments and arguments.

3. The rejection of claims 25-30 under 35 U.S.C. 103(a) as being unpatentable over Takahara et al., in view of Gibbons is withdrawn in view of applicant's amendments and arguments.

4. The rejection of claims 31 and 32 under 35 U.S.C. 103(a) as being unpatentable over Takahara et al., in view of Gibbons, in further view of Ono et al., is withdrawn in view of applicants amendments and arguments.

New Grounds For Rejection
Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 33-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a new matter rejection.

Applicants have added new claims with a preamble drawn to a method for increasing immunological reactivity of a polypeptide in agglutination immunoassays; comprising binding a nucleic acid to said polypeptide. Applicants point to support in on pages 27-29, example 5 of the instant specification, however it appears that the amendment lacks support. There is no teaching of a method to increase immunological reactivity of a polypeptide in an agglutination immunoassay. The specification states that the reactivity is shown in Table 2, but there is no teaching of a method or method steps that increase the immunological activity of a polypeptide in an agglutination immunoassay. Applicants have not pointed to support for a method increasing immunological reactivity of a polypeptide in an agglutination immunoassay by page and line number. Therefore, the claims are rejected for incorporating new matter.

Claims 25-40 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claims 25-32 are drawn to an agglutination immunoassay for assaying an antigen comprising binding a nucleic acid to a polypeptide; fixing the nucleic acid-bound polypeptide on the surface of a particle; contacting the antigen with the antibody; and detecting the resultant antigen-antibody complex. Claims 34-40 are drawn to a method for increasing immunological reactivity of a polypeptide in an agglutination immunoassay, comprising binding a nucleic acid to a polypeptide. The claims fail to recite critical and essential method steps required to practice the invention, therefore the claims are not enabled for the following reasons.

The invention requires a nucleic acid binding motif in the target polypeptide or a fusion protein with the target polypeptide, yet the claims fail to require a nucleic acid binding motif. Typically, an agglutination assay requires a bivalent binding moiety or the antigen can not be cross-linked thereby causing agglutination of a particle, however the claims fails to recite such a binding moiety. The method steps for merely contacting and detecting the antigen-antibody complex fails to recite how the agglutination can occur. The claims fail to recite method steps for how the nucleic acid is bound to one terminus of the polypeptide. The claims fail to employ a test sample in the method for assaying for an antigen. The claims fail to recite method steps that teach how to determine agglutination, which are critical or essential steps required to practice the invention not recited by the claims. Moreover, claim 33 fails to recite any method steps involved in a method for increasing immunological reactivity of a polypeptide in an agglutination immunoassay. Besides lacking the essential and critical steps as recited above, the claim further fails to recite how to increase the immunological reactivity. As recited

above, the missing steps create gaps in the instant invention as claimed. The specification teaches the recited steps, see examples 2-10, including centrifugation steps and the use of sucrose density gradients, however the claims do not positively recite the method steps in the body of claims. The claims do not teach steps that recite how to increase the immunological reactivity as recited by the preamble of the claim. The instant invention cannot be practiced without a complete recitation of the disclosed method steps. There is no correlation between the agglutination and determining an increase of immunological reactivity of a polypeptide. Therefore, the claims are rejected because the fail to recite necessary method steps.

It is known for agglutination assay methods to comprises a reaction medium comprising sample, a plurality of particles having a binding pair member bound to the surface of the particles and an analyte binding partner and detecting the presence of agglutination of the particles in the reaction medium. See Gibbons (US Patent 4,829,011). Without the essential and critical steps recited by the claims, the effects of the method for assaying for an antigen in an agglutination immunoassay are largely unpredictable.

Thus the appropriate steps must be recited in order to enable one of ordinary skill in the art to practice the invention. Therefore, the recitation lacks essential method steps and thereby results in an unpredictable and unreliable method that cannot be practiced; or in an unpredictable and therefore unreliable correspondence between a method for increasing immunological reactivity of a polypeptide in an agglutination immunoassay. Thus the claims lack support regarding utility and/or enablement.

Applicants have not recited method steps for an agglutination immunoassay for assaying an antigen or a method for increasing immunological reactivity of a polypeptide in an agglutination immunoassay, thus it is not clear that the alleged methods will actually produce agglutination. Absent clear demonstration of the methods steps in an agglutination assay, the methods can not be used in any well-established manner for assaying for an antigen or for increasing immunological reactivity of a polypeptide in an agglutination immunoassay. In absence of further guidance from Applicants, the skilled artisan would have to discover what the appropriate method steps, substrates are, the conditions, reagents. Such experimentation requires ingenuity beyond that expected of one of ordinary skill in the art. Such need for non-routine experimentation demonstrates that the specification is not enabled for any asserted use or well-established use for bacterial membrane polypeptides. Accordingly, the specification is not enabled for using the alleged agglutination immunoassay in any manner disclosed.

6. Claims 25-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 25 is unclear and confusing. It is unclear how to perform the agglutination immunoassay for assaying for an antigen when there is no sample being assayed. It is unclear how to perform the agglutination immunoassay for assaying an antigen when the assay already comprises an antigen. Furthermore, it appears that all the results performed by said methods would always be positive since the agglutination immunoassay already comprises an antigen, i.e., detection of the

antigen-antibody complex occurs in all assays according to the steps of this assay; thus it appears that this is a competition inhibition assay, i.e., the absence of agglutination is indicative of the presence of antigen. Therefore, the claim is unclear and confusing.

X It is unclear how to define "an antibody corresponding to said antigen", thus it is unclear what the antigen binds too. Does it bind to the nucleic acid or the polypeptide? It is unclear how to define corresponds to. The language recited by the claims does not allow one to be able to determine the metes of bounds of the claimed language.

The claim is drawn to an agglutination immunoassay comprising either a polypeptide or an antibody corresponding to said antigen; however the methods steps for performing the immunoassay, steps (i) and (ii), do not recite the use of the polypeptide or both the polypeptide and antibody. It should be noted that steps (A) and (B) are not considered method steps for assaying for an antigen. Furthermore, it is unclear how the polypeptide functions in the immunoassay. The claim also recites, X "wherein said immunoassay further comprises" however it is unclear how the immunoassay can further comprise steps when no previous assay steps have been recited.

The goal of the preamble of the claim does not correspond to the method steps recited in the claim, i.e., the goal appears to be performing an agglutination immunoassay, however there is no recitation of steps that recite how to determine agglutination, no reagents are required to be employed by the method steps, there is no centrifugation step, therefore, it appears that the method steps as recited are not

capable of performing an agglutination immunoassay for assaying for an antigen. Moreover, it is unclear how the polypeptide if the preamble cause agglutination.

Claim 25 recites the limitation "said antigen" in the claim. There is insufficient antecedent basis for this limitation in the claim.

Claim 26 is vague and indefinite. The claim is vague as to how a nucleic acid is bound to at least one terminus of the polypeptide. It appears that the only disclosed means is a fusion partner with a N or C terminal to the polypeptide that has a binding motif or nucleic acid binding motif that is internal to the polypeptide; however the claim fails to recite method steps for how a nucleic acid is bound to at least one terminus of the polypeptide.

In claim 33, the goal of the preamble of the claim, a method for increasing immunological reactivity of a polypeptide in an agglutination immunoassay, does not correspond to the method steps recited in the claim, i.e., the goal appears to be increasing immunological reactivity of a polypeptide, however there is no recitation of steps that recite how to increasing immunological reactivity or how the agglutination assay is performed. There are no reagents are required to be employed by the method steps, there is no centrifugation step, therefore, it appears that the method steps as recited are not capable of increasing immunological reactivity of a polypeptide in an agglutination immunoassay.

Claims 33-40 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. In claim 33 there are no steps; there is no to which binds the nucleic acid bound polypeptide to the surface of a particle; there is no contact step to contact the antigen with the antibody; there are no reagents named within the method steps, there is no centrifugation step; there is no detection of agglutination; and there are no steps to recite how to determine agglutination. Thus, the claim is rejected for failure to recite any method steps.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 33-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Thomas et al., (US Patent 4,749,647). Thomas et al., (US Patent 4,749,647) teach methods for a general method for the detection and measurement of analytes in a sample (col. 6 lines 40-43). Such interaction or association between different analytes is amenable to detection and measurement using different sets of recognition pairs (col. 8 lines 55-59). For example, specific DNA/protein interaction can be assayed under appropriate conditions using a labeled antibody to the protein analyte and a labeled probe for the DNA analyte, one of the two labels being a monomer and the other, a

reporter (col. 8 lines 60-65). In general, such determination requires cross-linking of the protein(s) to the nucleic acid and fragmentation of the nucleic acid prior to the assay (col. 8 lines 65-68). Thomas et al., teach immunoassays of the present invention can be performed in any of several configurations (col. 9 lines 3-5). Specific binding to polymer particles after incubation which would allow binding to occur; washing of the particles if necessary can occur, however measurement of the amount of reporter associated with the particle can occur or the particles can be separated from solution (col. 9 lines 50-63). Example V teaches analyte association assays including synthesis and monomerization of analyte detecting sequences. While example V-E teach an assay for p19 protein binding to Rous Sarcoma Virus-RNA (RSV-RNA). This would be a nucleic acid bound polypeptide. The inventors teach using a fluoresceinated anti-p19 antibody to detect the mixture (col. 43 lines 31-32). Thus the antigen is contacted with an antibody. Under this system, fluorescence is incorporated into the polymer particles (col. 43 lines 40-41). Two controls were run, which showed that there was substantially less incorporation of fluorescence into the polymer particles, indicating that both p19 protein and RSV-RNA are required for incorporation of the reporter in to the polymer (col. 43 lines 46-49).

It should be noted that the recitation an agglutination immunoassay or a method for increasing immunological reactivity of a polypeptide in an agglutination immunoassay has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it merely recites the purpose of a process or the intended use of a structure, and where

the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951).

Therefore, Thomas et al., teach an agglutination immunoassay or a method for increasing immunological reactivity of a polypeptide in an agglutination immunoassay comprising binding a nucleic acid to a polypeptide, fixing the nucleic acid bound polypeptide on the surface of a particle; contacting the antigen with a n antibody and detecting the resultant antigen-antibody complex as claimed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is (703) 305-0487. The examiner can normally be reached on Monday through Thursday from 6:30am to 4:00pm. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Ja-Na Hines
May 30, 2002

PATRICIA A. DUFFY
PRIMARY EXAMINER